

In re Application of DEBINSKI, ET AL.  
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AUG 11 2006

### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Listing of Claims:

Claim 1. (Currently Amended). A method for detecting glioblastoma multiforme in a brain tissue sample, the method comprising the steps of:

- (A) providing the brain tissue sample; and
- (B) contacting the brain tissue with a labeled antibody that binds specifically to human VEGF-D protein, a native human VEGF-D protein or a homology domain of human VEGF-D; and,
- (C) ~~analyzing~~ detecting the brain tissue for overexpression of VEGF-D, in the brain tissue as compared to normal brain tissue.

Claim 2. (Withdrawn). The method of claim 1, wherein the step (B) of analyzing the brain tissue sample comprises comparing the quantity of expression of the VEGF-D marker to a first sample known to express detectable levels of the VEGF-D marker and a second sample known to not express detectable levels of the VEGF-D marker.

Claim 3. (Withdrawn). The method of claim 1, wherein the VEGF-D marker is a VEGF-D nucleic acid.

Claim 4. (Withdrawn). The method of claim 3, wherein the VEGF-D nucleic acid is an RNA.

Claim 5. (Withdrawn). The method of claim 3, wherein the VEGF-D nucleic acid is a native VEGF-D nucleic acid.

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Claim 6. (Withdrawn). The method of claim 3, wherein the step (A) of providing a tissue sample comprises obtaining the brain tissue sample from a human subject; and the step (B) of analyzing the brain tissue sample comprises isolating RNA from the tissue sample, generating cDNAs from the isolated RNA, amplifying the cDNAs by PCR to generate a PCR product.

Claim 7. (Withdrawn). The method of claim 3, wherein the step (A) of providing a brain tissue sample comprises obtaining the tissue sample from a human subject; and the step (B) of analyzing the brain tissue sample comprises isolating nucleic acid from the tissue sample, and contacting the isolated nucleic acid with an oligonucleotide probe that hybridizes under stringent hybridization conditions to the VEGF-D nucleic acid.

Claim 8. (Withdrawn). The method of claim 7, wherein the oligonucleotide probe further comprises a detectable label.

Claim 9. (Currently Amended). The method of claim 1, wherein the VEGF-D ~~marker~~ protein is a native VEGF-D protein.

Claim 10. (Previously presented). The method of claim 9, wherein the VEGF-D protein is a full-length native VEGF-D protein.

Claim 11. (Original). The method of claim 9, wherein the VEGF-D protein is a proteolytic cleavage product of a VEGF-D precursor protein.

Claim 12. (Original). The method of claim 11, wherein the proteolytic cleavage product comprises a VEGF-D homology domain.

Claim 13. (Currently amended). The method of claim 9, wherein the step (A) of providing a brain tissue sample comprises obtaining the brain tissue sample from a human subject wherein said brain tissue sample comprises a glioblastoma multiforme cell exhibiting abnormal ploidy for chromosome X; and the step (B) of ~~analyzing~~ detecting overexpression of

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VEGF-D in said brain tissue sample comprises contacting at least a portion of said brain tissue sample with a probe that specifically binds to the VEGF-D protein wherein said probe is a monoclonal antibody or polyclonal antibody.

Claim 14. (Original). The method of claim 13, wherein the probe comprises a detectable label.

Claim 15. (Cancelled).

Claim 16. (Cancelled).

Claim 17. (Cancelled).

Claim 18. (Previously presented). The method of claim 13, wherein the monoclonal antibody is an anti-VEGF-D antibody that specifically binds human VEGF-D or a homology domain of human VEGF-D.

Claim 19. (Withdrawn). A method of modulating VEGF-D gene expression in a brain cancer cell comprising the steps of:

- (A) providing a brain cancer cell that expresses a VEGF-D gene; and
- (B) introducing into the cell an agent that modulates the expression of the VEGF-D gene in the cell.

Claim 20. (Withdrawn). The method of claim 19, wherein the agent is an oligonucleotide.

Claim 21. (Withdrawn). The method of claim 19, wherein the agent is an antisense oligonucleotide.

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Claim 22. (Withdrawn). The method of claim 21, wherein the antisense oligonucleotide hybridizes under stringent hybridization conditions to a polynucleotide that encodes a VEGF-D protein.

Claim 23. (Withdrawn). A method of identifying a test compound that modulates expression of a VEGF-D gene in a brain cancer cell, the method comprising the steps of:

- (A) providing a brain cancer cell expressing a VEGF-D gene;
- (B) contacting the cell with the test compound; and
- (C) detecting a modulation in the expression of the VEGF-D gene, wherein detecting the modulation indicates that the test compound modulates expression of the VEGF-D gene.

Claim 24. (Withdrawn). The method of claim 23, wherein the cell is derived from a tissue sample isolated from a human brain.

Claim 25. (Withdrawn). The method of claim 23, wherein the step of detecting the modulation in the expression of the VEGF-D gene comprises analyzing the cell for a change in the amount of a VEGF-D marker in the cell.

Claim 26. (Withdrawn). The method of claim 25, wherein the VEGF-D marker is a VEGF-D nucleic acid.

Claim 27. (Withdrawn). The method of claim 26, wherein the VEGF-D nucleic acid is an RNA.

Claim 28. (Withdrawn). The method of claim 26, wherein the VEGF-D nucleic acid is a native VEGF-D nucleic acid.

Claim 29. (Withdrawn). The method of claim 25, wherein the VEGF-D marker is a VEGF-D protein.

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Claim 30. (Withdrawn). The method of claim 29, wherein the VEGF-D protein is a native VEGF-D protein.

Claim 31. (Withdrawn). The method of claim 29, wherein the VEGF-D protein is a proteolytic cleavage product of a VEGF-D precursor protein.

Claim 32. (Withdrawn). The method of claim 31, wherein the proteolytic cleavage product comprises a VEGF-D homology domain.

Claim 33. (Withdrawn). A method for inhibiting angiogenesis associated with a brain cancer in a subject, the method comprising the steps of:

(A) providing a molecule that interferes with VEGF-D binding to a VEGF-D receptor; and

(B) administering the molecule to the central nervous system of the subject in an amount effective to inhibit blood vessel development associated with the brain cancer.

Claim 34. (Withdrawn). The method of claim 33, wherein the molecule specifically binds VEGFR-2.

Claim 35. (Withdrawn). The method of claim 33, wherein the molecule specifically binds VEGFR-3.

Claim 36. (Withdrawn). The method of claim 33, wherein the molecule specifically binds VEGF-D.

Claim 37. (Withdrawn). The method of claim 33, wherein the molecule is an antibody.

Claim 38. (Withdrawn). The method of claim 37, wherein the antibody is a polyclonal antibody.

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Claim 39. (Withdrawn). The method of claim 37, wherein the antibody is a monoclonal antibody.

Claim 40. (Withdrawn). The method of claim 39, wherein the monoclonal antibody is VD1.

Claim 41. (Withdrawn). The method of claim 37, wherein the antibody specifically binds to the VEGF-D protein.

Claim 42. (Withdrawn). The method of claim 37, wherein the antibody specifically binds to VEGFR-2.

Claim 43. (Withdrawn). The method of claim 37, wherein the antibody specifically binds to VEGFR-3.

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